Society for Clinical Data Management
DATA DRIVEN

SCDM 2016

INDIA CONFERENCE

9 - 10 December, 2016 | Hyderabad

Case Study 1

‘Reducing SDV doesn’t work!’ (Therefore RBM doesn’t work)’

What was the expectation?

- Saved CRA costs
- Saved traveling and logistics costs
- Quicker trial timelines and saved site costs
- Simplified process flow
- Less rigidly controlled sites

Desired Effect

- ✓ Quicker timelines
- ✓ Cost savings
- ✓ Happier sites

What was the actual result?

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More incorrect data in the clinical database.

More queries and delays in query responses

Overall milestone delays

Increased pressure on site

Frustration at sites over increased amount of work and sponsor complaints regarding site deficiencies

Overall Effect

- Decreased trial efficiency
- Higher costs
- Greater stress

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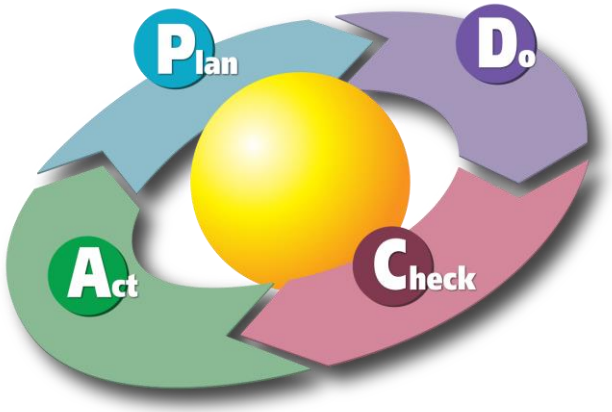
So what went wrong?

Lack of a scientific, process driven approach

Lack of a clear vision

- To create more reliable trial outcomes
- To reduce costs ***through increased efficiency***
- To reduce risk and stakeholder liability

No focus on 'PLAN'!



Ok. But what does 'PLAN' mean?

- The only way to extract the value RBM offers:
- The only way to save time and money:
- The only way to ensure higher quality data:
- The only way to make sure a good molecule makes it to the market:
- ***The only way to move forward:***

is to ***CONDUCT A RISK ASSESSMENT***

How do you conduct a Risk Assessment?

The easiest way is to start with a **checklist**

Risk Parameter	Risk Assessor Response	Please add comments/important information	Overall Risk Based on IPD worksheet(1-5) 1 – Low 3 – Significant 5 – Critical
Is the site new?Y/N	No		Answer all bullet points below
For sites used before, rate past performance from 1-10 :			
Adherence to data entry timelines (comment specifically on AEs and SAEs)	8		2
Number of queries	-	Metrics not available	No rating
Average query TAT	7		2
Quality Issues previously reported for the site	5		3
Are site staff familiar with policies and SOPs?	No	Due for training by CRA before enrolment	3
Has a protocol training been conducted by sponsor or Clin Ops?	Yes		Go to next question
If so, Is a training evaluation available?	No		3.5

15/25 = Risk rating 60%. Moderate - SDV plan 2

Risk Parameter	Risk Assessor Response	Please add comments/important information	Overall Risk Based on IPD worksheet(1-5) 1 – Low 3 – Significant 5 – Critical
Is the site new? **Y/N**	Yes		5
For sites used before, rate past performance from 1-10 :		**NA**	
Adherence to timelines	-		
Number of queries	-		
Average query TAT	-		
Quality Issues previously reported for the site	-		
Are site staff familiar with policies and SOPs?	No	Due for training by CRA before enrolment	3
Has a protocol training been conducted by sponsor or Clin Ops?	Yes		Go to next question
If so, Is a training evaluation available?	No		5

13/15 = Risk rating 86.67%. High - SDV plan 1

Snapshot of RACT criteria

Category Number	Category	Objective	Questions for Discussion	Considerations	Impact 3 point scale (blue line = category summary)	Probability 3 point scale (blue line = category summary)	Detectability 3 point scale (blue line = category summary)	Total Category Risk Score
4.4	Subject Population		How specific are the eligibility criteria?	Consider ability to document requirements/verify inclusion/exclusion criteria. Consider stratification based on subject population. What is required in terms of documentation for diagnosis? Consider clarity on central vs. local lab results being acceptable for inclusion/exclusion ranges.				#N/A
4.5	Subject Population		Will subjects be allowed to be rescreened if they do not pass all eligibility criteria?	Consider situations to allow rescreening. Consider ways to track subjects that are rescreened.				#N/A

Case Study 2

‘A much needed molecule may never reach the market simply because trial **risks** went **undetected**.’

What was the problem with the trial?

Database not designed to capture information necessary for end point analysis

Primary End Point:	→	Best Overall Response
What is required to calculate Best Overall Response:	→	Target Lesions, **Non-target lesions**, new lesions
What the CRF was designed to capture:	→	Target lesions, New lesions

What went wrong?

Formal protocol review? ***Not planned***

QC check for database design as per protocol? ***Not planned***

Expert review before database launch? ***Not planned***

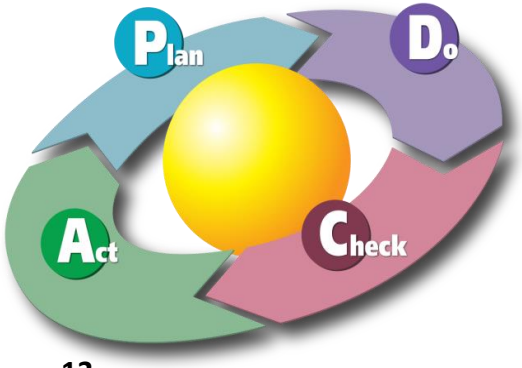
Periodic/interim review of datasets to assess end points? ***Not planned***

No QA processes built in at the PLANNING stage

What does QA have to do with RBM anyway?

Quality Assurance

- **Objective:** Lessen chances of deviations from the set standard.
- **Methodology:** Systemization. Step-by-step approach.
- **Focus:** Plan, Check, ACT
- **Expected outcome:** Achievement of set standard



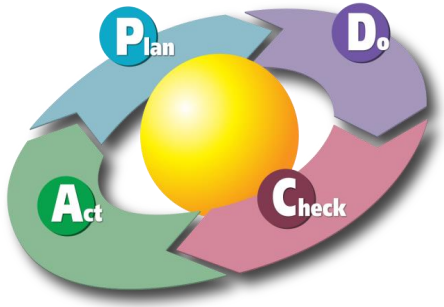
Risk Based Monitoring

- **Objective:** Identify 'effect of uncertainty on objectives'
- **Methodology:** Risk identification, analysis, evaluation, mitigation
- **Focus:** Plan, Check, ACT
- **Expected outcome:** Achievement of objectives **despite uncertainty**

RBM uses the **Cycle of Continual improvement to assure** the **quality** of trial outcomes.

A case of informal, unstructured RBM

No formal risk assessment PLAN.
No identification of critical data.



NO CHECKS (other than audit), therefore no ACT.

9 months into the 30-month trial, this discrepancy was highlighted during the internal audit, allowing corrective action to be taken, at great energy, rework and cost, but in time to ensure the trial was not completely wasted.

Case Study 3

Using technology to support risk monitoring

Monitoring for Risk Identification

A quarterly Risk Assessment review aimed at determining data authenticity indicated inaccurate data entry might be at play.

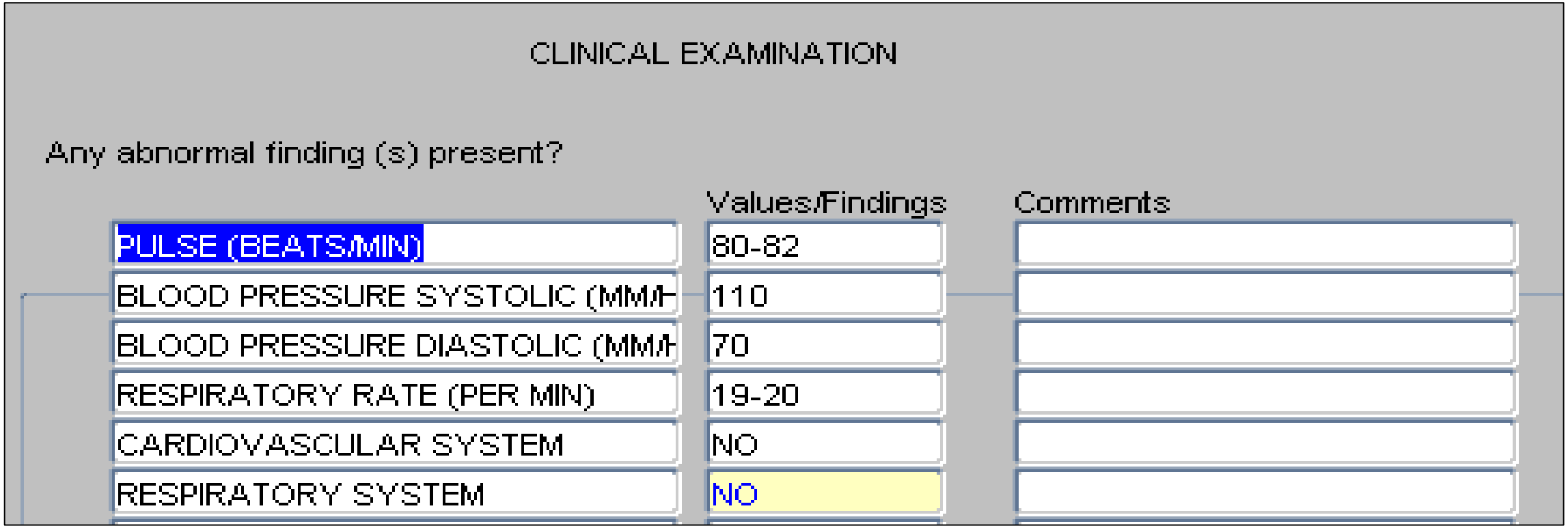
The database was set up to visualize how many times Query X had been answered by a data amendment rather than a response/explanation.

17 instances.

Query X raised across 6 sites.

Site 3 had data point amendments 100% of the time.

Monitoring for Risk Identification



CLINICAL EXAMINATION

Any abnormal finding (s) present?

	Values/Findings	Comments
PULSE (BEATS/MIN)	80-82	
BLOOD PRESSURE SYSTOLIC (MM/H	110	
BLOOD PRESSURE DIASTOLIC (MM/H	70	
RESPIRATORY RATE (PER MIN)	19-20	
CARDIOVASCULAR SYSTEM	NO	
RESPIRATORY SYSTEM	NO	

Monitoring for Risk Identification

CARDIO VASCULAR SYSTEM	YES	IHD, ACUTE INFERIOR WALL MI, HTN.	NO		NO		YES		YES	HTN

Please refer to the cell with data in bold: Original data on the CRF was 'Yes'. Upon querying, 'Yes' was changed to 'No' within the database. However, subsequent visit is again marked as 'Yes'. This is being highlighted to the sponsor from a risk management perspective.

The power of RBM to ensure authentic data

DOING RBM RIGHT

The Project Status Update for the fortnight indicated this as a risk to the sponsor.

Further, the DM team raised queries asking for reconfirmation of data changes for all instances.

Monitoring indicated that, two months later, Site 3 had fallen in line with the other 5 sites.

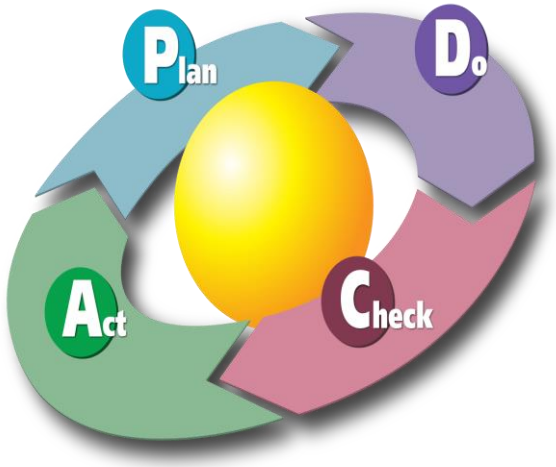
For a successful RBM methodology

PLAN

- A formal risk assessment and risk mitigation document needs to form the basis of all RBM strategies and actions you decide to adopt. **Identify critical data.**

CHECK

- Monitor regularly, for implementation against the plan, as well as for currency of the plan.



RBM is a dynamic process. Information review and recourse is essential to fully extracting its true value.

For a successful RBM methodology

RBM depends on smart technology AND smart people

- One in isolation of the other and you may not see the same degree of reliable data that allows effective drugs to alleviate the suffering they otherwise could.

RBM is a process for fact based decision making

- If it not working for you, look to see what you might not have got right just yet.

Is your RBM methodology SMART enough to succeed?

S pecific	Is your Risk Management Plan clear?
M easurable	Are metrics used for real time decision making?
A chievable	Are all stakeholders on the same page? How often do you need to remind/retrain them?
R elevant	Site specific, study specific, competence specific, work ethic specific issues addressed by RAMP?
T imebound	Do you review resultant metrics regularly enough to bring things back on track?

Do you use automation and visualization to keep your risk assessment *current?*